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Inside This Issue

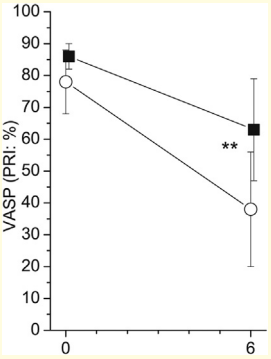
STATE-OF-THE-ART PAPER

CLINICAL RESEARCH

(continued on page A-18)

ANTITHROMBOTIC THERAPY

Morphine Reduces Effectiveness of Clopidogrel Loading Dose 630



Eva-Luise Hobl, Thomas Stimpfl, Josef Ebner, Christian Schoergenhofer, Ulla Derhaschnig, Raute Sunder-Plassmann, Petra Jilma-Stohlawetz, Christine Mannhalter, Martin Posch, Bernd Jilma

Hobl and colleagues investigated whether morphine administration affects the pharmacokinetics and pharmacodynamics of clopidogrel loading dose administration. Twenty-four healthy subjects received a loading dose of 600 mg clopidogrel together with placebo or 5 mg morphine intravenously in a randomized, double-blind, placebo-controlled, cross-over trial. Morphine injection delayed clopidogrel absorption and reduced the area under the curve levels of its active metabolite by 34%. Morphine delayed the maximal inhibition of platelet aggregation on average by 2 h. Morphine delays clopidogrel absorption, decreases plasma levels of clopidogrel active metabolite, and diminishes its effectiveness, which might lead to treatment failure in susceptible individuals.

CARDIOMETABOLIC RISK

Pulse Wave Velocity Improves CV Risk Prediction 636

Yoav Ben-Shlomo, Melissa Spears, Chris Boustred, Margaret May, Simon G. Anderson, Emelia J. Benjamin, Pierre Boutouyrie, James Cameron, Chen-Huan Chen, J. Kennedy Cruickshank, Shih-Jen Hwang, Edward G. Lakatta, Stephane Laurent, João Maldonado, Gary F. Mitchell, Samer S. Najjar, Anne B. Newman, Mitsuru Ohishi, Bruno Pannier, Telmo Pereira, Ramachandran S. Vasan, Tomoki Shokawa, Kim Sutton-Tyrell, Francis Verbeke, Kang-Ling Wang, David J. Webb, Tine Willum Hansen, Sophia Zoungas, Carmel M. McEniery, John R. Cockcroft, Ian B. Wilkinson

Ben-Shlomo and colleagues performed a systematic review and meta-analysis to determine whether aortic pulse wave velocity (aPWV) improves prediction of cardiovascular (CV) events beyond conventional risk factors. Individual participant data from 16 studies were combined, resulting in 17,635 participants, 10% of whom had a CV event. The pooled age- and sex-adjusted hazard ratio per SD change in log aPWV was 1.35 for coronary heart disease, 1.54 for stroke, and 1.45 for CV disease. Reclassification indexes showed that the addition of aPWV improved risk prediction. aPWV may enable better identification of high-risk populations who will benefit from more aggressive CV risk factor management.

Editorial Comment: Charalambos Vlachopoulos, Konstantinos Aznaouridis, Christodoulos Stefanadis, p. 647

(continued on page A-19)

CARDIOMETABOLIC RISK

Miklos Z. Molnar, Kamyar Kalantar-Zadeh, Evan H. Lott, Jun Ling Lu, Sandra M. Malakauskas, Jennie Z. Ma, Darryl L. Quarles, Csaba P. Kovesdy

Molnar and colleagues performed a retrospective chart review of almost 150,000 U.S. veterans with varying stages of chronic kidney disease (CKD) to assess the association between use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and mortality in CKD patients. ACEI/ARB administration was associated with a significantly lower risk of mortality both in the intention-to-treat analysis and in the as-treated analysis. The association of ACEI/ARB treatment with lower risk of mortality was present in all examined subgroups. In this large contemporary cohort of nondialysis-dependent CKD patients, ACEI/ARB administration was associated with greater survival.

Editorial Comment: Kevin Damman, Hiddo J. Lambers-Heerspink, p. 659

HEART FAILURE

Tonje Thorvaldsen, Lina Benson, Marcus Ståhlberg, Ulf Dahlström, Magnus Edner, Lars H. Lund

Thorvaldsen and colleagues assessed observed and expected all-cause mortality in 10,062 patients with New York Heart Association (NYHA) functional class III to IV heart failure (HF) and ejection fraction (EF) <40% registered in the Swedish Heart Failure Registry. Five pre-specified universally available risk factors were assessed using multivariable Cox regression: systolic blood pressure ≤90 mm Hg, creatinine ≥160 μmol/l, hemoglobin ≤120 g/l, no renin-angiotensin system antagonist, and no β-blocker. For patients age ≤80 years, the presence of 1, 2, or 3 to 5 of these risk factors conferred an independent hazard ratio for all-cause mortality of 1.40, 2.30, and 4.07, and a 1-year survival of 79%, 60%, and 39%, respectively. The authors conclude that for patients age ≤80 years with NYHA functional class III to IV HF and EF <40%, mortality is predominantly related to HF or its comorbidities. Patents with ≥1 of these risk factors may benefit from either heart transplant/mechanical assist device or potential palliative care and thus may benefit from referral to an advanced HF center.

(continued on page A-20)

HEART RHYTHM DISORDERS

ECG Criteria for RVH Lack Sensitivity 672

Isaac R. Whitman, Vickas V. Patel, Elsayed Z. Soliman, David A. Bluemke, Amy Praestgaard, Aditya Jain, David Herrington, Joao A. C. Lima, Steven M. Kawut

Current electrocardiographic (ECG) criteria for right ventricular hypertrophy (RVH) were based on cadaveric dissection in small studies. Whitman and colleagues assessed the diagnostic properties of ECG criteria for RVH measured by cardiac magnetic resonance imaging (cMRI) in adults without clinical cardiovascular disease. Traditional ECG criteria were specific (many >95%) but had low sensitivity for RVH by cMRI. The positive predictive values were not sufficiently high as to be clinically useful (maximum 12%). Classification and regression tree analysis revealed that no combination of ECG variables was better than the criteria used singly. These results show that the recommended ECG screening criteria for RVH are not sufficiently sensitive or specific for screening for mild RVH in adults without clinical cardiovascular disease.

PERIPHERAL VASCULAR DISEASE

Statin Use Associated With Reduced MACCE in Patients With Chronic Limb Ischemia 682

Gregory G. Westin, Ehrin J. Armstrong, Heejung Bang, Khung-Keong Yeo, David Anderson, David L. Dawson, William C. Pevec, Ezra A. Amsterdam, John R. Laird

While statin medications are recommended for secondary prevention in patients with peripheral arterial disease (PAD), their effectiveness in patients with chronic limb ischemia (CLI) is uncertain. Westin and colleagues performed a retrospective chart review of 380 CLI patients. A total of 65% of patients were prescribed statins. After propensity weighting, statin therapy was associated with lower 1-year rates of major adverse cardiovascular and cerebrovascular events (MACCE) (stroke, myocardial infarction, or death) (hazard ratio [HR]: 0.53), mortality (HR: 0.49), and major amputation or death (HR: 0.53). Statin use was also associated with improved lesion patency among patients undergoing infrapopliteal angioplasty. These robust, although nonrandomized, results suggest that there are significant benefits for statin use in patients who present with CLI.

Editorial Comment: Michael R. Jaff, p. 691